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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/464,426	12/16/99	STALGIS C	IN09640

HM12/0118

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EXAMINER	
FOLEY,S	
ART UNIT	**PAPER NUMBER**
1648	2

DATE MAILED: 01/18/01

Please find below and/or attached an Office communication concerning this application or pr ceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/464,426	STALGIS ET AL.	
	Examiner	Art Unit	
	Shanon A. Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-37 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-37 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78).

Specification

Throughout the specification and the claims the word "alpha" is repeatedly misspelled as "alfa". According to Webster's dictionary, alfa is a communications word for the letter "a". The disclosure is directed to treating disease, not radio communication. Appropriate correction is required.

In addition, page 2, line 24, has a couple of typos, "treatmen", should be "treatment" and "agreater" should be "a greater".

Claim Objections

Many claims have misspelled "alpha" to "alfa".

Claims 5, 10-20, 36, and 37 are objected to because of the following informalities:

Claim 5, line 28, "aboujt" is misspelled and is presumably "about".

In claims 10-20 have the abbreviation, "BIW". Each abbreviation should be spelled out at its first instance in the claims to eliminate any possible confusion as to the meaning of the terms.

Claim 18, line 20, "by20" is presumably "by 20".

Claim 36 is followed by claim number 36, and should be renumbered as claim 37.

Appropriate correction is required.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-36 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-69 of copending Application No. 09/311487. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. The claims in the instant application are drawn to treating hepatitis C patients with ribavirin and the same kinds of inteferon alpha derivatives in the same treatment regiments.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-36 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-43 of U.S. Patent No. 09/464425. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in the instant application are drawn treating hepatitis C patients with ribavirin and interferon alpha derivatives for the same treatment regiments. Substituting non-pegylated interferon alpha for treatment and the instant application would be an obvious choice for one of skill in the art.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim1 recites "a therapeutically effective induction dosing amount of interferon-alpha". What is being induced? This affects all dependent claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for administering pegylated interferon alpha 2 or 3 times a week, does not reasonably provide enablement for administering pegylated interferon alpha once a week. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to a method of treating patients with hepatitis C by administering 400-1200 mg per day of ribavirin and 0.5-1.5 mg/kg of pegylated interferon once a week. Pegylated interferon was developed to reduce dosing frequency to treat chronic hepatitis C. The state of the prior art indicates that pegylation of interferon does not change intrinsic pharmacodynamic parameters, and based on mathematical modeling, it was predicted that the clinical response would decrease the dosing frequency from twice a week to three times a week, but not down to once a week. This prediction was later confirmed by the results from a phase II HCV study with six dosage regiments. See Xu et al., the entire abstract. Based on the teachings of the reference, one skilled in the art would doubt a method of treating HCV by administering pegylated interferon once a week. There is no existence of a working example provided in the specification that would enhance the predictability of using pegylated interferon (in conjunction with ribavirin) once a week. Therefore, based on the state of the art that demonstrates the inability of pegylated interferon to be effective against HCV when administered once a week, the lack of guidance and working examples, undue experimentation would be required of the skilled artisan to use the claimed invention in its full scope.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chemello et al., Grint et al., and Gilbert et al.

The claims are drawn to a method of treating patients having chronic hepatitis C, genotypes 1-3, by administering 400-1600 mg of ribavirin and 0.5 to 1.5 mg or 20 to 250 mg of pegylated interferon-2a or pegylated interferon alpha-2b for 36-44 weeks to maintain no detectable HCV-RNA for at least 24 weeks at the end of treatment.

Chemello et al. teaches administering 15 mg/Kg of ribavirin per day and 3 MU of natural interferon alpha 3 times a week for 6 months (Group C) to patients with HCV. At the end of the treatment period, HCV-RNA was negative in 66.6% of Group C. HCV genotyopes were defined in all patients and normalization of ALT was observed in 55% of cases with HCV-2 or HCV-3 and 12% in those patients with HCV-1. Chemello et al. does not teach particular desired forms of interferon alpha that includes the pegylated forms of interferon or administering treatment longer than 24 weeks, or 6 months.

Grint et al. teaches treating chronic hepatitis C patients who are previously untreated, non-responsive treatment patients, and patients who were previously treated with a monotherapy, but have relapsed. The treatment consists of administering 400-1000 mg per day of ribavirin and interferon alpha 1-3 million IU weekly, five times a week, or daily for 6-12 months to increase efficacy in treating hepatitis C while alleviating side effects observed in monotherapy treatment with ribavirin or interferon alpha due to the strong dosage or the extended duration. See the detailed description in columns 1-4 and claims 1-20. Grint et al. indicates that the interferon alpha and ribavirin dosage is subject to change, based on the requirements of the patient. This is demonstrated in claims 4, 5, 13, and 14, where the interferon-alpha dosage is anywhere from 1-3

million IU weekly, five times a week, or daily for 6-12 months. The dosage amounts claimed by Grint et al. provide one of ordinary skill in the art a guideline to follow for administering the drugs. It is a well-established practice in the medical arts to optimize dosage, depending on the specific needs of the patient. One of ordinary skill in the art at the time the invention was made would have been motivated to extend treatment duration and beyond 24 weeks due to the observations made in hepatitis C genotypes made by Chemello et al., with the added benefits of alleviating side by administering lower doses for a longer period of time taught by Grint et al. Grint et al does not teach the pegylated forms of interferon alpha.

Gilbert et al. (WO 95/13090) disclosed improved formulations of interferon alfa-2a and interferon alfa-2b, wherein they are conjugated to a polyethylene glycol polymer, the so-called pegylated interferons. Gilbert et al. disclose that these pegylated forms of interferon alpha retain all of the biological activity as the unconjugated forms, and that the pegylated forms are longer acting, offering great improvement over the natural short action of interferon alpha. Similar dosages are used by Gilbert et al. for in vivo applications, from $1x10^5$ to $1x10^7$ IU. The dosages of the conjugate administered would be based on the clinical experience of the practitioner and the treatment indication, as it is an established practice in the medical arts to optimize dosage for the treatment of disease. Gilbert et al. indicates that these long-acting interferon alphas would be useful in treatment of certain viral infections, including HCV (page 12, line 19 through page 13, line 7). Gilbert et al. has taught a way for even further improvement of the already established therapies taught by the references that would have been obvious for one of ordinary skill in the art at the time the invention was made to employ since the ultimate goal in all of the teachings is to improve available treatment.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to elongate the time of therapy with the combination treatment, as prolonged therapy would appear to provide additional rate of success, taught by Grint et al. One would have been motivated to elongate the treatment time, in view of the results obtained from the different HCV-infected patients taught by Chemello et al., and increase treatment courses of up to 18 months with different dosages, depending on the requirements of the patients, taught by Grint et al. and Gilbert et al. A reduction of side effects from the drugs is an added benefit to the treatments taught by Grint et al. It would have been obvious to one of ordinary skill in the art at the time the invention was made would have been further motivated to select and evaluate the pegylated interferon alfa-2a or –2b of Gilbert et al. for use in the protocol of Chemello et al. and Grint et al. Gilbert et al. discloses that the pegylated forms offer uniform activity, are longer acting in vivo, and are useable for the treatment of chronic HCV infection. One of ordinary skill in the art would have been motivated to select the pegylated interferons for use in those same methods because of the improved properties of the pegylated forms. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon A. Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on 7:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Shanon Foley
August 7, 2001